American Red Cross

National Headquarters

December 21, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Room 1-23
Rockville, MD 20852

RE: Requirements for Testing Human Blood Donors for Evidence of Infection Due to Communicable Disease Agents and Requirement for Blood, Blood Components, and Blood Derivatives; Proposed Rule. [64 Fed. Reg. 45339 (August 19, 1999) (Docket No. 98N-0581)]

Dear Docket Officer:

This letter is to provide public comments on behalf of the American Red Cross (ARC or Red Cross) concerning the Food and Drug Administration's (FDA or Agency) Proposed Rule on Requirements for Testing Human Blood Donors. Specifically, FDA is proposing to

> revise the general biological product standards by updating the hepatitis B virus (HBV) and human immunodeficiency virus (HIV) testing requirements, by adding testing requirements for hepatitis C virus (HCV), human T-lymphotropic virus (HTLV), and by adding requirements for licensed supplemental (i.e., additional, more specific) testing when a donation is found to be repeatedly reactive for any of the required screening tests for evidence of infection due to communicable disease agents.

The regulation also proposes several new requirements for shipping of untested blood products/components and for testing autologous units.

The Red Cross, through its 37 Blood Services regions, supplies approximately 46% of the nation's blood component transfusion needs. We recognize fully that a comprehensive set of testing regulations is an appropriate step for the Agency to take to help ensure the safety of the blood supply. We also appreciate the efforts that have been undertaken by FDA to prepare these regulations, given their complexity and the comprehensive nature of the proposal. Below, ARC provides our views for the public record, and hope that our information will aid the Agency in its decision making on these important requirements.

98N-0581

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Exceptions

The proposal contains a discussion of the exceptions FDA is considering under this rulemaking. Specifically, page 45343 states:

> FDA is requesting comment on whether to exempt from testing... each donation of dedicated apheresis donors. ... to permit testing proposed in sec. 610.40(a) ... only once at the beginning of a 30-day period of donation by a dedicated apheresis donor for a single recipient.

ARC agrees with and encourages FDA to implement this exception and believes there are appropriate reasons for its adoption.

Recently implemented new tests, such as Nucleic Acid Testing (NAT), have added substantially to the reliability of test results. If the donation is going to test positive for the disease marker, it is more likely to be accurately detected immediately, with testing of the first donation, then ever before. For subsequent donations, the donor is still subject to the health history and lifestyle screening questions. Thus, changes that may have occurred that might make the donor unsuitable, are likely to be detected through the screening.

We also believe this exemption is advisable for clinical reasons. Examples include cases where the transfusion is for emergency purposes, or if the testing is delayed due to a weekend or holiday when test facilities are unavailable, the recipient may still receive the benefit of a directed donation without the delay of waiting for the test results necessary for non-directed donations.

ARC has one additional comment. Specifically, we encourage FDA to consider extending the exclusion to other directed blood components. For example, directed donations where the intended purpose is for the manufacture of red cell or plasma products or from parent to child may also be desirable under the same circumstances surrounding directed apheresis donations. These donations could be appropriately managed under this same exclusion clause with no further risk than what would be experienced by the apheresis transfusion recipients.

Release or Shipment Prior to Testing

On page 45344, Section F, FDA proposes a new requirement for approval under Section 610.40(e) when certain routine shipments are taking place. Specifically:

> FDA is proposing... to permit, with FDA approval, routine shipment of certain blood components for further manufacturing before testing is completed and the tests results are received by the collection facility... the agency would expect the collection facility and the manufacturing facility ... to submit with their request specific procedures for collection, shipment, and quarantine of a product before testing is completed. Once the procedures have been approved, manufacturers may then begin to ship products prior to the completion of testing.

It is ARC's belief that this new requirement will not contribute to the Agency's intentions i.e. "to ensure the continued availability of biological products... which require rapid preparation from blood." ARC acknowledges that there are some products for which shipment of donations for further manufacture must take place rapidly, for example, due to the need to begin the further manufacture while the product is fresh. We also agree that rapid shipment, sometime prior to the receipt of test results, must take place in order to ensure appropriate manufacture. However, we do not know of any data or circumstances where review of the information FDA now wishes to receive, or a lack of FDA review, have contributed to or held back a prompt delivery and further manufacture of the blood product.

Nor is there a public health concern since *the units are not being shipped for transfusion,* rather, they are being shipped for further manufacture. If a positive test result is found during or after shipment, the manufacturer will receive immediate notification and the product(s) undergoing further manufacture will not be shipped from the manufacturer to the consignee. Thus, plans and procedures submitted to FDA under such a requirement should not need more than a 30 day review period and should be granted an automatic approval at that time.

Additionally, FDA's action to require an additional submission to the agency which they will then review and "approve", could have the opposite effect from what is intended. The delay in waiting for FDA review and approval, which has sometimes been measured in months or in years, may impede the blood establishment's ability to rapidly prepare biological products, rather than facilitate it. The Agency has worked very diligently and successfully towards improving turn around time for review of licensure submissions. However, these new submissions may once again stress their review process.

We assume that FDA expected this to be a one-time submission outlining the procedures for all firms for which further manufacturing arrangements exist. If not, potential delays in FDA's review and approval will be intensified by the additional, separate submissions for each manufacturer.

ARC urges FDA to delete this requirement. If there are still concerns about the blood establishments' plans and procedures, all such procedures are available upon request by FDA investigators during their inspections. Thus, FDA has full oversight and opportunity to review all plans without risk of encountering potential delays during an "approval" process.

Restrictions on Shipment or Use

On page 45344, Section G, FDA describes instances where there are additional new requirements for FDA approval. Specifically, the FDA indicates that:

> Under proposed Sec. 610.40(f)(2)(ii), blood establishments intending to ship or use human blood or blood components for further manufacture that test repeatedly reactive when screened for evidence of infection due to a communicable disease agent ... would apply for approval by FDA...
>
> If repeatedly reactive blood or blood components are to be used for further manufacturing into injectable products, the blood or blood component would be required to be labeled with the exempted use specifically ... Distribution may not commence until approval is granted.[1]

ARC's concern with these new requirements is that there does not appear to be a distinct description of the problems previously encountered that these new requirements are intended to correct. There is a discussion of labeling requirements. However, all such products which test repeatedly reactive are already labeled, packaged, and shipped according to FDA, Department of Transportation (DOT) and Occupational Safety and Health Administration (OSHA) safe shipping and handling regulations. The preamble does not compare the new regulations with the already existing ones from other agencies, and specific instances of shipping problems known to FDA have not been discussed in the preamble. As a consequence, the additional health or safety benefit that will be provided by these regulations is not evident.

[1] ARC assumes that FDA intends that the manufacture into noninjectable products, such as in vitro diagnostic products, of units that test repeatedly reactive would be covered by the provisions in proposed Sec. 610.40(f)(2)(ii).

An even greater concern is the potential delay in receiving "approval" by FDA. The potential delay in approval, and therefore the manufacture of the blood products, could impede maintaining the availability of the blood supply and biologics products. This concern is of special importance when the approval requirement overlaps with existing ones, does not have a well defined added benefit, and the information that would be reviewed is already available to FDA investigators upon request during inspections. ARC recommends modifying this requirement to allow submission to FDA with an automatic approval.

Future Rulemakings

ARC has a general comment regarding FDA's plans for future testing regulatory requirements. On page 45341 of the Preamble, the Agency states:

> FDA is considering proposing a general testing regulation for blood and blood components in the future that would require blood establishments to test for additional relevant communicable diseases. Such a rule could impose testing obligations as additional relevant communicable disease agents are identified and FDA approves tests for such agents.

One possible interpretation of this statement is that that the Agency is considering development of a regulation that will require implementation of each test *automatically* upon receipt of an FDA approved license. ARC agrees that all tests should be *considered* for implementation. However, if an automatic inclusion is being contemplated, we urge FDA to reconsider this approach.

Each test and each communicable disease should be addressed on a case by case basis, and any rulemaking that requires their implementation should be subject to appropriate notice and comment under the Agency's Good Guidance Practices and the Administrative Procedures Act.

Also, ARC anticipates that each test and each communicable disease will be different enough to warrant individual consideration. Numerous factors could vary including availability of a suitable number of test kits, availability of laboratory space and appropriate laboratory design, quality control issues, Clinical Laboratories Improvement Act (CLIA) regulations, designation of funding for the tests, and staff training to conduct and evaluate the test results. All of these should be fully evaluated, and the public given ample opportunity to comment, prior to including any new test as a regulatory requirement.

Syphilis Testing

ARC supports FDA's efforts to review relevant data and consider eliminating the requirement for syphilis testing. ARC also acknowledges that sufficient data will be required as described in section A on page 45342 and 45343:

> If the agency receives comments with adequate data ... FDA may proceed with rulemaking to remove the requirements for a serologic test for syphilis...

Red Cross has begun research that we believe will support this step. Our initial efforts were described at length at FDA's meeting on this proposal held on November 22, 1999. In addition, we have attached the data and a description to this letter for additional review by FDA.

Conclusion

The Red Cross appreciates the opportunity to submit its views on these regulations to FDA. If there are any questions on this letter, please contact Anita Ducca, Director, Regulatory Relations, at 703-312-5601. If there are any questions regarding the attached data and research pertaining specifically to syphilis testing, please contact Roger Dodd at 301-738-0641.

Sincerely,

Glenn M. Mattei, Esq.
Senior Director
Quality Assurance and Regulatory Affairs
Biomedical Services,
American Red Cross

Attachments

The following attachment has been submitted to Docket number 98N-0581.

It is also being submitted to Docket No. 98N-0607.

Syphilis Testing

ARC supports FDA's efforts to review relevant data and consider eliminating the requirement for syphilis testing. ARC also acknowledges that sufficient data will be required as described in section A on p. 45342 and 45343:

> If the agency receives comments with adequate data ... FDA may proceed with rulemaking to remove the requirements for a serologic test for syphilis...

Red Cross has begun research that we believe will support this step. Our initial findings were presented at FDA's meeting on this proposal held at NIH on November 22, 1999, and at a private meeting with FDA/CBER staff on December 15, 1999. We have provided a summary description of our findings below and have attached copies of our presentation materials for additional review by FDA.

We recognize that accurately assessing the value of blood donor serological testing for syphilis in relation to transfusion safety and public health will require extensive quantitative data from multiple sources. Our concerns with blood donor syphilis testing in its present format primarily arise from the very poor predictive value of the test for active syphilis infection. As a result, a very difficult and upsetting result notification message that must be provided to the vast majority of seropositive donors who have never had syphilis infection, or experienced infection many years ago that has long since been treated.

The aspects of this issue that we have explored include: 1) the prevalence of reactive screening tests and positive confirmatory tests among blood donors in our system; 2) the extent to which FTA-ABS confirmed serology among random blood donors does, or does not reflect the presence of circulating T. pallidum DNA; and 3) the relationship of a reactive syphilis serological screening test to unreported behavioral risk in active donors. In the interest of increasing the scientific knowledge base about the potential for transfusion-transmitted syphilis in the US, ARC is willing to consider the funding and implementation of additional studies to expand our current pilot data regarding infectivity of seropositive donor samples, as evidenced by the presence of T. pallidum DNA and RNA. As discussed during the 12/15 meeting with CBER staff, a final sample size for these studies of n = 1000 samples will constitute a sample that is likely to provide infectivity estimates that are reasonably reliable from a statistical standpoint. To examine the possibility of a surrogate relationship between blood donor syphilis seropositivity and infection with other transfusion-transmissible infection, the ARC ARCNET program has also begun an analysis of its systemwide epidemiologic database to determine the extent to which syphilis seropositivity is predictive of prevalent and/or incident HIV, HTLV, HCV, and HBV infection.

Blood Donor Syphilis Testing in the ARC System
Susan Stramer, Ph.D, ARC National Confirmatory Testing Laboratory

All donated blood is screened for total antibody to T. pallidum by PK-TP (PK7200 Olympus). Repeatedly reactive samples are confirmatory tested by FTA-ABS (Zeus) to an interpretation of Positive (2-4+), Minimally Reactive (1+), or Negative. Non-negative samples are then tested by RPR to assist donor notification of test results. Trends in seroprevalence for each of these assays are provided in the attached data sheets.

Relationship of anti-HBc and Serologic Tests for Syphilis (STS) to Blood Donor Behavioral Risk Factors. A.E. Williams, K. Watanabe, D. Ameti, S. Kleinman, M. P. Busch, S. Orton, G. J. Nemo. NHLBI REDS Study, Rockville, MD

Donor screening tests for anti-HBc and STS have limited value for prevention of post-transfusion hepatitis B and syphilis. It is unknown whether these tests have any value for identification of unreported donor risk behaviors. Anonymous mail surveys to measure donor characteristics and deferrable risk (DR98) were administered to 92,581 recent donors at eight blood centers from 4/98 through 10/98. The survey sample was weighted to over-represent anti-HBc+ and STS+ donors and surveys were pre-coded to reflect these results. Odds ratios comparing DR98 among anti-HBc+ and STS+ donors vs. seronegative donors were tested by Chi-Sq.

DR98 prevalence among respondents (weighted data) was 2.9% among 50,267 seronegative donors, 8.0% among 1726 anti-HBc+ donors (OR=2.9; $p< 0.001$), and 13.7% among 414 STS+ donors (OR=5.5; $p<0.001$). When the donor screening questions related to history of syphilis or treatment for syphilis were removed from the deferrable risk calculation however, deferrable risk in STS+ donors was no higher than the risk in seronegative controls. Because STS+ and anti-HBc+ seroprevalence in the donor pool is low (0.14% and 0.7% respectively), these tests eliminate only a small proportion of total deferrable risk in the unscreened donor pool (1.0% and 2.2% respectively).

Prevalence of *T. pallidum* DNA in the Blood of Donors Who Are Confirmed Positive by Current Serological Tests for Syphilis
SL Orton, MSPH, PhD candidate, RG Cable, MD, AJ Grindon, MD
AE Williams, Ph.D. American Red Cross ARCNET Program
Hsi Liu, Ph.D, Centers for Disease Control and Prevention

Based upon the hypothesis that the blood of STS reactive, FTA-ABS reactive donors does not differ from seronegative controls in terms of syphilis infectivity, our study goal was to determine (on a pilot basis) whether STS reactive, FTA-ABS reactive donors showed any evidence of circulating *T. pallidum* DNA. The sample size tested included 100 STS reactive, FTA-ABS samples; 50 of which were RPR reactive, 50 RPR nonreactive. Aliquots from existing platelet concentrates (PC) from these donors were tested for *T. pallidum* DNA using two PCR test methodologies. The first PCR test is specific for *T. pallidum* and sensitive to 25 organisms per 100 ul of extracted material; the second PCR test is a multiplex test that includes testing for *T. pallidum* DNA and is sensitive to 10 organisms per 100 ul of extracted material. Negative and positive external controls were tested. The positive external control was prepared by spiking a 100 ul sample aliquot from an STS nonreactive platelet concentrate with ~50 organisms. All 100 samples were negative for *T. pallidum* DNA by both PCR tests, and all external control results were appropriate. The study had several limitations which included (1) fresh whole blood is a preferable sample, although PC's were adequate for this study, (2) DNA testing cannot differentiate between live and dead organism (not relevant to these results) and (3) in a study of sample size 100 and all negative test results, there is up to a 3% chance that there is an incorrect interpretation of no infectivity. We concluded that we could not demonstrate circulating *T. pallidum* DNA in STS reactive, FTA-ABS positive blood donors. Further work will include RT-PCR testing for RNA (a more sensitive methodology), and should include further study with a larger sample size.

Prevalence of circulating *T. pallidum* DNA in STS+/ FTA•ABS + blood donors:

- American Red Cross ARCNET Program
  - SL Orton, MSPH, PhD candidate
  - RG Cable, MD
  - AJ Grindon, MD
  - AE Williams, Ph.D.
- Centers for Disease Control and Prevention
  - Hsi Liu, Ph.D.

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Factors that influence an infected individual (with spirochetemia) presenting as a blood donor include:

Symptomatology

Incidence

Background

- Primary syphilis: chancre/acute local lymphadenopathy present (97%/80%) ~ 3 weeks after exposure with subsequent organism infiltration of the blood stream. Resolution of the chancre occurs at ~ 6 weeks.
- Secondary syphilis: infiltration of the blood stream (and peak spirochetemia) causes systemic macropapular rash development in ~ 100% of infected individuals (~ 6 weeks after exposure), with gradual clearing of the spirochete.

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The phases overlap.

continued

- It is unlikely that an individual would be asymptomatic during spirochetemia.
- Rabbit infectivity tests indicate that with disappearance of overt symptoms, the blood loses its ability to infect due to migration of the spirochete to the lymphoid tissue.
- STS are positive except very early in the primary phase.

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continued

- CDC reported that in 1998:
  - 87% decline in incident syphilis cases between 1990 (20.6/100,000) and 1998 (2.6/100,000)
  - 14 states reported < 5 cases; 5 states reported 0 cases
  - 78% (2430/3115) US counties reported 0 cases
  - 50% of incident cases occurred in 0.9% (31/3115) US counties

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ARC statistics

- 1,801,505 allogeneic donations tested by PK-TP (after diluent modification) between May 1993 and September 1995; representing 16% of total blood collected
- 2151 (0.12%) STS reactive; 1274 (0.07%) confirmed by FTA-ABS
- 6,000,000 donations annually:
  - ~7,200 lost components
  - ~4,200 temporarily deferred donors

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How does syphilis testing impact the ARC?

This data is extracted from a paper by Aberle-Grasse (ARCNET) in Transfusion, 2/99

Goal

Determine if there is any evidence of circulating *T. pallidum* in the blood of donors who are STS reactive, FTA-ABS reactive.

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Methods: ARC laboratory infectivity study

- Target sample size: 100 STS reactive, FTA-ABS reactive donations; 50 RPR reactive, 50 RPR non-reactive (including 16 autologous)
- Collect and freeze daily (within ~24 hours) any existing platelet concentrates from PK-TP (Olympus Corp) reactive blood donations. Ship to HL.
- Upon receipt of confirmatory test results, aliquot platelets and send for DNA testing (maximum of 2 freeze/thaw cycles).

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NE: MA, ME, VT, NH:	5 samples
CT:	7
Southern: GA, South Florida	23, 52
GCP: DC, MD	13

Testing

- PCR for *T. pallidum* specific DNA
  - pol A gene target: 378 bp band
  - capillary electrophoresis and fluorescent detection
  - read on an ABI 310 Genetic Analyzer
  - sensitivity as low as 25 organisms/100 ul platelet concentrate extracted

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continued

- Multiplex PCR kit (Roche) for *T. pallidum, H. ducreyi* and Herpes Simplex Virus type 1 and 2.
  - 47kd basic membrane protein gene target for *T. pallidum* previously described.
- Both assays included internal and external control samples. Positive external controls were diluted to 50 organisms per 100 μL from stock *T. pallidum* (Nichols strain) cultures.

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Same sample volume was used.

Results

- All 100 samples tested negative for *T. pallidum* DNA by both assays.
- Internal and external control samples results were appropriate.

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Study limitations

- The optimal sample is fresh whole blood.
- One weakness of DNA detection is the inability to differentiate live from dead organisms.
- Because we can never "prove" a negative test result, in a pilot study with a sample size of 100 and all negative test results, there is up to a 3% chance that there is an incorrect interpretation of no infectivity.

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The spirochete can tolerate ~3% oxygen tension and then will die ~12 hours. The oxygen tension of the platelet concentrate bag is ~15%. This is probably not the component we should be concerned about.

For the purposes of our study, however, the slow spin separation of platelet rich plasma followed by the hard spin preparation of the platelet concentrate would yield spirochetes in the platelet concentrate bag. In addition, *T. pallidum* DNA is an extremely stable biopolymer.

Conclusions

- We did not demonstrate circulating *T. pallidum* DNA in STS reactive, FTA-ABS reactive blood donors in this study.
- Because of the low incidence of syphilis in the population, it is unlikely that an infected individual would present as a blood donor.

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From the literature:

The low incidence of disease in the US population (and the demographics of individuals currently found to be infected with syphilis) make it unlikely that an infected individuals will present as a blood donor.

Conclusions continued

- It is unlikely that a symptomatic individual would present as a blood donor.
- The data suggests that in the absence of syphilis testing, transfusion transmitted syphilis infection is unlikely to occur.

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From the literature:

Due to the symptomatology of this disease during peak spirochetemia (secondary phase), it is unlikely that a symptomatic individual would donate.

AND

Current information regarding spirochete survival (or lack thereof) in the various blood components, coupled with a lack of evidence that confirmed positive blood donors actually have spirochetemia, makes the potential risk of transfusion transmitted syphilis small.

Relationship of anti-HBc and Serologic Tests for Syphilis (STS) to Blood Donor Behavioral Risk Factors

AE Williams, K Watanabe, DI Ameti,
S Kleinman, MP Busch, S Orton, GJ Nemo

Retrovirus Epidemiology Donor Study (REDS)

Background - anti-HBc

- Assays for anti-HBc have low specificity and high donor loss (0.7 - 1.8%) when used for screening of donated blood
- Value of anti- HBc for detection of HBV infection is limited
- Surrogate value of anti-HBc for behavioral risk detection is speculative

Background - STS

- Current STS assays detect long term *T. pallidum* antibodies in 0.1 - 0.2% of healthy blood donors.
- No well-documented cases of transfusion-transmitted syphilis have occurred in the US in over 30 years
- Surrogate value of STS for behavioral risk detection is speculative

Background - STS (cont.)

- 1995 NIH Consensus Conference debated the value of continued blood donor STS screening
- August 1999: FDA seeks data regarding the value of donor STS (Proposed Rules: Requirements for testing....)
  - as a marker of high risk behavior
  - as a surrogate test for other infectious diseases
  - in preventing the transmission of syphilis through transfusion

Study Objective

- Assess the value of anti-HBc and STS as surrogate indicators of blood donor risk behaviors

REDS 1998 Donor Survey

- ARC, Greater Chesapeake and Potomac Region
- ARC, Southeastern Michigan Region
- ARC, Southern California Region
- Blood Centers of the Pacific - Irwin/UCSF
- Oklahoma Blood Institute
- New York Blood Center
- Blood Bank of San Bernardino
- Lifeblood (Memphis)

- Medical Coordinating Center - Westat, Inc.

REDS 1998 Donor Survey (cont.)

- Anonymous mail survey
- Allogeneic donors; ≥18 years.
- Monthly probability sample of donors April through October 1998.
- 92,581 sampled donors at eight sites
- 57% survey response rate

REDS 1998 Donor Survey (cont.)

- Survey sample included four laboratory test strata:
  - anti-HBc+
  - STS+
  - other lab reactivity
  - seronegative
- all anti-HBc+ and STS + donors surveyed

REDS 1998 Donor Survey - Content

- Demographics
- Donation history/experiences
- Deferrable Risk Assessment (DR)
- Multiple Investigations
  - » Surrogate value of STS and anti-HBc
  - » Incentives
  - » Hemochromatosis
  - » HIV test-seeking

Deferrable Risk

- A risk that should have resulted in deferral according to blood donor screening criteria at the time of the survey

Results: Deferrable Risk (DR)

	DR Prev	OR	Adj.OR*
◆ Neg	2.9%	1.0	1.0
◆ anti-HBc	8.0%	2.9†	2.7†
◆ STS+	13.7%	5.4†	5.5†
◆ Other+	11.5%	4.4†	3.3

* Odds ratios adjusted for gender, age, race/ethnicity, education, center, FT donors (all $p < .001$)

† $p < 0.001$

Proportion of Overall DR Associated with anti-HBc and STS (%)

	DR Prev	% of Overall DR
◆ Neg	2.9	94.4
◆ anti-HBc	8.0	2.4
◆ STS+	13.7	1.0
◆ Other+	11.5	2.2

Proportion of Overall MSM and IDU Risks Associated with anti-HBc and STS (%)

	MSM	s/MSM	IDU	s/IDU
◆ Neg	94.1	96.5	87.0	93.7
◆ anti-HBc	3.0	2.1	2.5	1.9
◆ STS+	0.3	0.5	0.2	0.5
◆ Other+	2.6	1.0	10.3	3.9

STS-Related Risks Included in Deferrable Risk Calculation

Q48. In the past 12 months, have you had a positive test for syphilis?

Q49. In the past 12 months, have you had or been treated for syphilis or gonorrhea?

Results: Deferrable Risk (DR) excluding STS

	DR Prev	OR	Adj.OR*
◆ Neg	2.7%	1.0	1.0
◆ anti-HBc	7.3%	2.8†	2.5†
◆ STS+	4.7%	1.7‡	1.3
◆ Other+	11.5%	4.6†	3.6‡

* Odds ratios adjusted for gender, age, race/ethnicity, education, center, FT donors (all $p < .001$)

† $p < 0.001$; ‡ $p < 0.05$

Summary: Surrogate value of anti-HBc+

- When controlled for FT donor status and demographic factors, anti-HBc+ donors have a 2.7-fold higher level of reported deferrable risk than seronegative donors.
- Qualitatively, anti-HBc-associated risks are similar to those of the overall donor base
- When anti-HBc prevalence (0.7%) is considered, anti-HBc+ is associated with 2.4% of overall DR

Conclusion: Surrogate value of anti-HBc+

- The value of anti-HBc as a surrogate needs to be considered in the context of other variables that have modestly higher levels of deferrable risk. (males, FT donors, etc.)

Summary: Surrogate value of STS

- When controlled for FT donor status and demographic factors, STS+ donors have a 5.2-fold higher level of reported deferrable risk than seronegative donors.
- When STS+ prevalence is considered (0.14%), STS is associated with 1.0% of overall DR)

Summary - Surrogate value of STS (cont.)

- However, deferrable risk associated with STS+ is largely due to STS-related risk factors.
- When STS-related risk factors are not considered, STS has no significant value as a surrogate indicator of behavioral risk

Conclusion

- **If molecular studies continue to show an absence of *T pallidum* in STS+ blood, the requirement for STS testing of donated blood should be removed.**

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